

File Number: 96-41D1
Filing Date: March 3, 2000
Express Mail Label No. EL488339843US

UNITED STATES PATENT APPLICATION

OF

Stephen R. Jaspers, Katherine H. Sprugel, Hong Ping Ren,
Jacqueline M. Humes, Ross C. Hoffman, Darrell C. Conklin

FOR

~~COMPOSITIONS AND METHODS FOR STIMULATING PANCREATIC ISLET CELL~~
~~REGENERATION~~

BFB
10/29/03
undt B

~ ZINS1 POLYPEPTIDE COMPOSITION
STIMULATING PANCREATIC ISLET GROWTH

808
10/29/03
amalt B

ZINSA POLYPEPTIDE COMPOSITION
A STIMULATING PANCREATIC ISLET GROWTH

DESCRIPTION

5 ~~Compositions and Methods for Stimulating Pancreatic Islet
Cell Regeneration~~

BACKGROUND OF THE INVENTION

10 β -cells are specialized cells that secrete
insulin and are found in pancreatic islets. Insulin
belongs to a group of protein/polypeptide hormones.
Insulin increases the rate of synthesis of glycogen, fatty
acids, and proteins and stimulates glycolysis and cell
15 proliferation. It also promotes the transport of glucose,
and some other sugars, and amino acids into muscle and fat
cells. Insulin levels are regulated to maintain glycemic
homeostasis, and an important mechanism for regulating
insulin production, and hence insulin levels, is β -cell
20 mass.

During the lifetime of an individual metabolic
needs can change drastically, requiring dynamic changes in
cells and tissues that regulate homeostasis. During
pregnancy (Marynissen et al., Diabetes 36:883-891, 1987)
25 β -cell mass increases, as well as in response to obesity
(Kloppel et al., Surv. Synth. Pathol. Res. 4:110-125,
1985). These increases in β -cell mass are attributed to
an increased requirement for insulin to maintain normal
glucose levels (Parsons et al., Endocrinology 130:1459-
30 1466, 1992). It has also been shown that β -cell mass
normally decreases post-partum, primarily by apoptosis
(Scaglia et al., Endocrinology 136:5461-5468, 1995).

It is generally believed that increases in β -
cell mass occurs in three ways: 1) an increase in cell
35 size and function; 2) increased proliferation of mature β -
cells; and/or 3) increased recruitment and differentiation
of β -cell progenitors. In diabetic mice, animals that